Familiality of Quantitative Autism Traits

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Abstract

Background: Autistic traits exist along a continuum that extends into social functioning in the general population, and they aggregate in the family members of children with autism spectrum disorder (ASD). Quantitative measures are therefore essential when investigating the patterns of familiality of these traits. Prior studies have suggested differential inheritance patterns of autistic traits that depend on the cognitive level of the child with ASD as well as the family type.

Objective: Our goal was to examine the family patterns of quantitative autism traits (QAT) in a group of simplex autism families of high-functioning children with ASD.

Method: We used the Social Responsiveness Scale (SRS) to evaluate QAT in 47 ASD families and 46 control families. SRS assessments (parental/spousal evaluations) were collected for the children with ASD, their siblings, and their parents as well as for the control children and their parents.

Results: The SRS was able to distinguish individuals with ASD from the control children and from their unaffected siblings. Significant group differences were also found when comparing the fathers of ASD families to control fathers and when comparing the brothers of individuals with ASD to control boys, with male members of ASD families having higher SRS scores. Gender differences were observed in the group of siblings of children with ASD and the group of parents of children with ASD, with males having higher scores than females. In ASD families, a positive trend between child and father QAT was found, whereas mothers’ scores were not associated with child outcomes. By contrast, in control families, mothers’ QAT correlated more strongly with child QAT.

Conclusions: Autistic traits aggregate in the fathers and brothers of children with ASD in simplex autism families. The QAT levels of the family members should be taken into consideration when planning the rehabilitation of the child or adolescent with ASD and when designing family interventions.

Keywords: autism spectrum disorder, autistic traits, quantitative autism traits, broader autism phenotype, Social Responsiveness Scale

Introduction

Autism spectrum disorder (ASD) is a childhood neurodevelopmental disorder that is defined by impairment in social development and communication as well as the presence of marked repetitive behaviors and narrow interests (1). There is wide variability in the phenotypic manifestation of ASD, but the central feature may be considered a deficit in reciprocal social behavior.
Familiality of QAT

The term reciprocal social behavior refers to the extent to which an individual can engage in emotionally appropriate, turn-taking social interaction with others. Reciprocal social behavior requires the individual to be cognizant of the emotional and interpersonal cues of others, to appropriately interpret and respond to those cues, and to be capable of emotional engagement (2). There is evidence that ASD traits are continuously distributed in the general population, genetically transmitted across generations, and aggregated at subclinical levels in relatives of individuals with autism (2-15). The phenotypic profile of subthreshold ASD traits that manifest in some relatives of autistic individuals has been referred to as the broader autistic phenotype (4); when measured by quantitative instruments, these broader deficits in social functioning are called quantitative autism traits (QAT) (13). The broader autistic phenotype has been thought of as an index of family genetic risk for autism (16).

Many family studies have used categorical definitions (i.e., present/absent) of the broader autistic phenotype in the same way that diagnostic classifications of ASD are categorical. However, given evidence that autistic traits exist along a continuum that extends into social functioning in general population and that these quantitative traits are strongly heritable, quantitative measures are essential when investigating patterns of family inheritance. The Social Responsiveness Scale (SRS) is a widely used quantitative questionnaire regarding autistic traits that reliably measures QAT and that yields a total score to quantify these traits (2).

Prior studies have suggested differential inheritance patterns of autistic traits that depend on both the cognitive level of the child with ASD (17) and the family type (i.e., simplex vs. multiplex) (13,14,18). In this study, our goal was to evaluate whether quantified autistic traits aggregate in and are correlated among family members in a sample of simplex families of high-functioning, school-aged children with ASD. We also sought to examine the familiality of subclinical QAT in the families of control children.

Methods
Participants
Participants were drawn from a clinically based molecular genetic study, the details of which have been previously reported (19). The study was conducted in 2003 in the Northern Ostrobothnia Hospital District area in the Providence of Oulu, Finland, and approved by the Northern Ostrobothnia Hospital District Ethics Committee. The target population included all elementary school-aged children 7 to 16 years old with the following characteristics: 1) they were outpatients who had been diagnosed with ASD at Oulu University Hospital; 2) they had undergone full-scale intelligence quotient testing that found them to be in the normal range; and 3) they carried no additional diagnoses of speech or language disorders, hearing impairments, or fragile X syndrome. The families of 60 children met the inclusion criteria and were invited to participate.

Invitation letters that included a preliminary fact sheet about the study protocol and objectives were sent to the parents of the children, and a time for a confirmatory phone call was scheduled in each letter. Psychologists (KJ or SKG) called the parents at the designated time to inquire about each family's willingness to participate in the study and to answer any questions the parents might have about the research. Parents were also asked whether they (or the school personnel familiar with their children) had concerns about their other children having ASD; the siblings of identified children with ASD were accepted into the proband group at this point. The SRS questionnaire and the Autism Spectrum Screening Questionnaire (ASSQ) (20,21) were sent to the parents of the families that were willing to participate. Parents were asked to complete both questionnaires for the evaluation of all of their children; the SRS was also used by each parent to evaluate the other parent. Written consent was obtained from all parents and from children who were more than 12 years old.

Families were subsequently invited to the Oulu University Hospital outpatient clinic, where confirmatory diagnostic assessments were performed. A single day was reserved for each child evaluation. The clinical diagnoses of the outpatients had previously been assigned on the basis of the diagnostic criteria regarding current behavior as defined by the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (22). In this study, diagnoses were reassigned with the use of the Autism Diagnostic Interview–Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS), and the early development of the children was checked with the use of their patient records. The ADI-R interviews of parents and the ADOS observations of children were administered by a clinical psychologist who had been trained in the use of these instruments for research purposes (KJ). After these investigations, diagnoses were redefined in detail on the basis of all available data (i.e., ADI-R and ADOS data as well as information from patient records), in accordance with the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria (23), and also after taking into account the development that occurred during the first 3 years of each child’s life. Consensus
diagnoses were established between the clinical psychologist (KJ) and a pediatrician who was clinically experienced in the autism field (M-LM). Diagnostic evaluations were also performed for all siblings of outpatients with ASD for whom parents had reported possible concerns about ASD.

Control children were recruited from two mainstream elementary schools in Oulu, Finland. One class of students from each of the first through ninth grades was randomly selected and invited to participate in the study with their families (210 students). Families of 88 students participated (82 families in total; six children were siblings from the same families). Controls were screened with the ASSQ, and those exceeding 7 points were excluded (24). We subsequently checked all potential participants’ hospital records to ensure that none of the control children were ASD outpatients at the Oulu University Hospital. At that time, the Oulu University Hospital was the only facility in the Northern Ostrobothnia Hospital District area where ASD diagnoses were made.

Individuals who did not meet publisher requirements for the scoring of the SRS (i.e., >10% missing items) were excluded, and only families with satisfactory SRS data from at least two family members (including the child with ASD or the control child) were included in analyses. Multiplex ASD families were also excluded (i.e., families with more than one child with ASD; this was a total of three families). The final study sample consisted of 47 ASD families and 46 control families (of which five included two control children).

Measures
The Autism Diagnostic Interview–Revised. The ADI-R (25) is a standardized, investigator-based, semi-structured parental interview that was developed to elicit the full range of information about the criteria necessary to evaluate and diagnose ASD. The ADI-R covers the main symptom areas associated with ASD, including reciprocal social interaction, communication, and restricted and stereotyped behaviors and interests.

The Autism Diagnostic Observation Schedule. The ADOS (26) is a semi-structured assessment of social interaction, communication, and play or imaginative use of materials. It comprises four modules that are based on the verbal level of the individual who is being evaluated.

Both the ADI-R and the ADOS make use of diagnostic algorithms that are based on separate thresholds for ASD symptom domains. The domain scores are the sums of codings that indicate the severity of impairment on the basis of symptom frequency and the degree of interference with daily living.

The Social Responsiveness Scale. The SRS (2,27) is a 65-item measure of autistic traits, which are rated on a Likert-type scale that ranges from 0 (not true) to 3 (almost always true). These questions yield a total continuous score (raw score range, 0 to 195) that can be interpreted as the level of QAT. SRS questions cover the dimensions of communication and the behavior characteristics of ASD. Subscales that represent different aspects of the capacity for reciprocal social behavior can also be obtained from the SRS: perception (Social Awareness, 8 items; raw score range, 0 to 24); cognition (Social Cognition, 12 items; raw score range, 0 to 36); communication (Social Communication, 22 items; raw score range, 0 to 66); motivation (Social Motivation, 11 items; raw score range, 0 to 33); and characteristic autistic preoccupations (Restricted Interests and Repetitive Behavior, 12 items; raw score range, 0 to 36) (2). The SRS is highly psychometrically sound, and it demonstrates excellent construct validity when compared with the ADI-R. Scores are unrelated to intelligence level or age (9,28).

The Autism Spectrum Screening Questionnaire. The ASSQ (20,21) is a 27-item parent or teacher-report inventory that is designed to screen for ASD in children with full-scale intelligence quotient ≥50. Of the ASD screening measures, the ASSQ is the only questionnaire that has been validated for Finland (24). The ASSQ covers the main areas of ASD (i.e., social interaction, communication, and restricted and repetitive behaviors) as well as motor deficits and behaviors (e.g., clumsiness) and other associated symptoms (e.g., motor and vocal tics). Items are rated on a 3-point Likert-type scale (i.e., 0 = normal, 1 = some abnormality, and 2 = definite abnormality), with total scores ranging from 0 to 54 and higher scores indicating more severe levels of social impairment.

Statistical Analyses
Analyses were performed with the SPSS statistics package version 17.0. For the replacement of missing data, the expectation–maximization algorithm imputation method was used for cases in which less than 10% of the SRS items were missing. To correct for skewed data regarding the SRS outcomes of the siblings and parents of children with ASD, we employed the non-parametric Mann–Whitney U test to examine group differences in SRS scores.

When investigating the familiality of the QAT, we first looked at the correlations between family members’ scores; specifically, we examined partial
correlations while controlling for the children’s ages. We subsequently conducted a quartile split of child SRS scores despite a known decrease in group sample size to graphically compare child–parent groups on the basis of high and low levels on the SRS. Box plots (Figure 1) were created to show the distributions of parent scores by child quartile.

**Results**

*Within-Group Differences in Social Responsiveness Scale Outcome Measures*

Gender differences in SRS scores emerged in the groups of siblings and parents of children with ASD.

In the sibling group, brothers of individuals with ASD had higher SRS total scores than the sisters of individuals with ASD (23.9 ± 23.2 vs. 12.2 ± 8.0; \( p = .032 \)). Brothers also had significantly higher scores (as compared with sisters) on the subscales of Social Cognition (4.3 ± 4.9 vs. 2.0 ± 1.3; \( p = .042 \)) and Social Motivation (5.5 ± 4.3 vs. 2.9 ± 2.7; \( p = .021 \)). No statistically significant gender differences were found in the SRS scores of the groups of children with ASD or the control children (see Table 1).

In the group of parents of children with ASD, fathers had significantly higher SRS total scores than did mothers (38.2 ± 29.6 vs. 24.1 ± 21.7, \( p = .014 \)). According to the SRS subscales, fathers also had significantly higher scores in the Social Awareness (5.2 ± 4.2 vs. 3.6 ± 3.0; \( p = .041 \)), Social Communication (13.0 ± 10.8 vs. 6.0 ± 7.6; \( p = .001 \)), and Restricted Interests and Repetitive Behavior subscales (6.2 ± 6.7 vs. 3.7 ± 4.3; \( p = .048 \)) as compared with mothers. No significant differences were found when comparing the fathers of control children with the mothers of control children (see Table 2).

*Between-Group Differences in Social Responsiveness Scale Outcome Measures: Children*

No statistically significant group differences emerged when examining the mean ages of the child groups (ASD probands: \( n = 47 \), 39 boys and 8 girls, age 11.3 ± 2.1 years; ASD siblings: \( n = 43 \), 23 boys and 20 girls, age 10.9 ± 2.3 years; controls: \( n = 51 \), 26 boys and 25 girls, age 11.3 ± 2.5 years). The SRS scores for the ASD probands were significantly higher as compared with their siblings and with control children when it came to the SRS total score as well as all of the SRS subscale scores (Table 3).

The brothers of children with ASD scored statistically significantly higher on the Social Motivation subscale as compared to control boys (5.5 ± 4.3 vs. 3.1 ± 2.1; \( p = .014 \)) (Table 1). Although the results were not statistically significant, brothers of individuals with ASD had higher SRS total scores than did control boys (23.9 ± 23.2 vs. 17.1 ± 8.9), with a mean difference in SRS scores of 6.8 and an effect size of 1.7 (very large).

The sisters of children with ASD had significantly lower scores on the Social Awareness and Social Cognition subscales as compared with the control girls (2.5 ± 1.7 vs. 3.8 ± 2.1; \( P = .025 \), and 2.0 ± 1.3 vs. 3.2 ± 1.8; \( p = .014 \), respectively) (see Table 1).

### Table 1. Social Responsiveness Scale Raw Scores of Siblings of Children With Autism Spectrum Disorder and Control Children by Gender

<table>
<thead>
<tr>
<th>Social Responsiveness Scale Scores (Mean ± Standard Deviation)</th>
<th>Brothetns of Children With ASD (n = 23)</th>
<th>Control Boys (n = 26)</th>
<th>Sisters of Children With ASD (n = 20)</th>
<th>Control Girls (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Score*</td>
<td>23.9 ± 23.2(^*)</td>
<td>17.1 ± 8.9</td>
<td>12.2 ± 8.0(^*)</td>
<td>18.1 ± 12.1</td>
</tr>
<tr>
<td>Social Awareness</td>
<td>3.9 ± 1.3</td>
<td>4.9 ± 1.9</td>
<td>2.5 ± 1.7</td>
<td>3.8 ± 2.1</td>
</tr>
<tr>
<td>Social Cognition</td>
<td>4.3 ± 4.9(^*)</td>
<td>3.4 ± 2.5</td>
<td>2.0 ± 1.3(^*)</td>
<td>3.2 ± 1.8(^*)</td>
</tr>
<tr>
<td>Social Communication</td>
<td>7.7 ± 8.5</td>
<td>5.6 ± 3.7</td>
<td>4.0 ± 3.3</td>
<td>5.9 ± 5.2</td>
</tr>
<tr>
<td>Social Motivation</td>
<td>5.5 ± 4.3(^*)</td>
<td>3.1 ± 2.1(^*)</td>
<td>2.9 ± 2.7</td>
<td>4.0 ± 3.2</td>
</tr>
<tr>
<td>Restricted Interests and Repetitive Behavior</td>
<td>2.5 ± 4.3</td>
<td>1.0 ± 1.2</td>
<td>0.9 ± 1.3</td>
<td>1.2 ± 1.7</td>
</tr>
</tbody>
</table>

\(^*\)\( p < .05 \) (two-tailed test);  
Brothers of Children With ASD > Sisters of Children With ASD for Total Score, Social Cognition, and Social Motivation; Brothers of Children With ASD > Control Boys for Social Motivation; Sisters of Children With ASD < Control Girls for Social Awareness and Social Cognition;  
ASD, Autism spectrum disorder
**Familial Associations between Social Responsiveness Scale Scores**

When investigating the familiality of the QAT, we first looked at the correlations between children’s SRS scores and those of their parents. Statistically significant positive correlations were observed between the SRS scores of children and their parents in all child groups (ASD probands, siblings, and control children), although these correlations were moderate. Partial correlation coefficients (controlling for child age) between child and parent SRS scores are presented in Table 4.

Despite a known decrease in the group sample sizes, to graphically compare child and parent scores on the basis of high and low levels on the SRS, we conducted a quartile split of children according to total SRS scores. We observed a positive trend in the families of children with ASD: the father’s SRS score increased as the child’s quartile increased (see Figure 1). No such trend was evident for mothers’ scores or among control children.

### Table 4. Social Responsiveness Scale Total and Subscale Raw Score Means by Parent Group

<table>
<thead>
<tr>
<th>Social Responsiveness Scale Scores</th>
<th>Fathers of Children With ASD (n = 44)</th>
<th>Control Fathers (Mean ± Standard Deviation)</th>
<th>Fathers of Children With ASD vs. Control Fathers (p Value)</th>
<th>Mothers of Children With ASD (n = 38) vs. Mothers of Children With ASD vs. Control Mothers (p Value)</th>
<th>Fathers of Children With ASD vs. Mothers of Children With ASD (p Value)</th>
<th>Control Fathers (p Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Score</td>
<td>38.2 ± 29.6</td>
<td>19.0 ± 13.4</td>
<td>.001</td>
<td>24.1 ± 21.7</td>
<td>21.3 ± 21.7</td>
<td>NS</td>
</tr>
<tr>
<td>Social</td>
<td>5.2 ± 4.2</td>
<td>3.5 ± 2.2</td>
<td>.019</td>
<td>3.6 ± 3.0</td>
<td>3.8 ± 5.0</td>
<td>NS</td>
</tr>
<tr>
<td>Awareness</td>
<td>7.2 ± 6.2</td>
<td>3.2 ± 2.8</td>
<td>.001</td>
<td>5.4 ± 5.0</td>
<td>3.8 ± 5.0</td>
<td>NS</td>
</tr>
<tr>
<td>Social Cognition</td>
<td>13.0 ± 10.8</td>
<td>6.5 ± 5.4</td>
<td>.001</td>
<td>6.0 ± 7.6</td>
<td>6.3 ± 7.6</td>
<td>NS</td>
</tr>
<tr>
<td>Social Communication</td>
<td>6.6 ± 5.3</td>
<td>4.2 ± 3.8</td>
<td>.017</td>
<td>5.5 ± 4.6</td>
<td>4.2 ± 4.6</td>
<td>NS</td>
</tr>
<tr>
<td>Social Motivation</td>
<td>6.2 ± 6.7</td>
<td>1.7 ± 1.6</td>
<td>.017</td>
<td>3.7 ± 4.3</td>
<td>2.7 ± 2.8</td>
<td>NS</td>
</tr>
<tr>
<td>Restricted Interests and Repetitive Behavior</td>
<td>6.2 ± 6.7</td>
<td>1.7 ± 1.6</td>
<td>.017</td>
<td>3.7 ± 4.3</td>
<td>2.7 ± 2.8</td>
<td>NS</td>
</tr>
</tbody>
</table>

Results obtained with the Mann–Whitney U test; NS, not significant

### Table 3. Social Responsiveness Scale Raw Scores of Child Groups

<table>
<thead>
<tr>
<th>Social Responsiveness Scale Scores (Mean ± Standard Deviation)</th>
<th>Children With ASD (47)</th>
<th>Siblings of Children With ASD (43)</th>
<th>Control Children (51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Score</td>
<td>92.1 ± 24.0</td>
<td>18.4 ± 18.6</td>
<td>17.6 ± 10.5</td>
</tr>
<tr>
<td>Social Awareness</td>
<td>10.8 ± 4.2</td>
<td>3.2 ± 2.8</td>
<td>3.9 ± 2.0</td>
</tr>
<tr>
<td>Social Cognition</td>
<td>17.6 ± 6.6</td>
<td>3.3 ± 3.8</td>
<td>3.3 ± 2.1</td>
</tr>
<tr>
<td>Social Communication</td>
<td>31.2 ± 5.8</td>
<td>5.9 ± 6.8</td>
<td>5.8 ± 4.5</td>
</tr>
<tr>
<td>Social Motivation</td>
<td>14.0 ± 3.5</td>
<td>4.3 ± 3.9</td>
<td>3.5 ± 2.7</td>
</tr>
<tr>
<td>Restricted Interests and Repetitive Behavior</td>
<td>18.6 ± 1.1</td>
<td>1.7 ± 3.3</td>
<td>1.1 ± 1.4</td>
</tr>
</tbody>
</table>

Results obtained with the Mann–Whitney U test; All p levels <.001 for Children With ASD versus Siblings of Children With ASD; All p levels <.001 for Children With ASD versus Control Children; All p levels non-significant for Siblings of Children With ASD versus Control Children; ASD, Autism spectrum disorder

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**Between-Group Differences in Social Responsiveness Scale Outcome Measures: Adults**

No statistically significant differences were found with regard to the ages of the parent groups (ASD parents: n = 85, age 41.5 ± 6.3 years; control parents: n = 81, age 41.3 ± 5.2 years). For the parent groups, the total SRS scores of fathers of children with ASD were statistically significantly higher as compared with the total SRS scores of the fathers of control children: SRS total score, 38.2 ± 29.6 versus 19.0 ± 13.4 (p < .001); Social Awareness, 5.2 ± 4.2 versus 3.5 ± 2.2 (p = .019); Social Cognition, 7.2 ± 6.2 versus 3.2 ± 2.8 (p < .001), Social Communication, 13.0 ± 10.8 versus 6.5 ± 5.4 (p < .001); Social Motivation, 6.6 ± 5.3 versus 4.2 ± 3.8 (p = .017); and Restricted Interests and Repetitive Behavior, 6.2 ± 6.7 versus 1.7 ± 1.6 (p < .001).

Mothers’ scores did not differ significantly for any of the SRS outcome measures (Table 2).
### TABLE 4. Partial Correlation Coefficients Between Child and Parent Social Responsiveness Scale Scores After Controlling for Age

<table>
<thead>
<tr>
<th></th>
<th>ASD Proband With ASD</th>
<th>Sibling of Child With ASD</th>
<th>Control Child</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>.55**</td>
<td>.39*</td>
<td>.43*</td>
</tr>
<tr>
<td>Mother</td>
<td>.17</td>
<td>.42*</td>
<td>.54**</td>
</tr>
<tr>
<td><strong>Social Awareness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>.59**</td>
<td>.39*</td>
<td>.43*</td>
</tr>
<tr>
<td>Mother</td>
<td>−.03</td>
<td>.26</td>
<td>.61**</td>
</tr>
<tr>
<td><strong>Social Cognition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>.59**</td>
<td>.44*</td>
<td>.35*</td>
</tr>
<tr>
<td>Mother</td>
<td>.12</td>
<td>.46*</td>
<td>.31*</td>
</tr>
<tr>
<td><strong>Social Communication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>.53**</td>
<td>.33</td>
<td>.40*</td>
</tr>
<tr>
<td>Mother</td>
<td>.23</td>
<td>.43*</td>
<td>.50**</td>
</tr>
<tr>
<td><strong>Social Motivation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>.20</td>
<td>.22</td>
<td>.17</td>
</tr>
<tr>
<td>Mother</td>
<td>.06</td>
<td>.30</td>
<td>.39*</td>
</tr>
<tr>
<td><strong>Restricted Interests and Repetitive Behavior</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>.51**</td>
<td>.40*</td>
<td>.20</td>
</tr>
<tr>
<td>Mother</td>
<td>.07</td>
<td>.29</td>
<td>.39*</td>
</tr>
</tbody>
</table>

*p < .05 (two-tailed test); **p < .01 (two-tailed test); ASD, Autism spectrum disorder.

### FIGURE 1. Distributions of Children With Autism Spectrum Disorder’s and Control Children’s and Their Parents’ Social Responsiveness Scale Total Raw Scores on the Basis of Child Quartiles of Social Responsiveness Scale Total Raw Scores

1. Lowest child quartile; 4, Highest child quartile; ASD, autism spectrum disorder; SRS, Social Responsiveness Scale.
Discussion

Our primary aim was to examine family patterns of the broader autistic phenotype by measuring QAT in the first-degree relatives of children with ASD with the use of the SRS questionnaire. We have previously found the Finnish SRS to be a valid measure for differentiating children with ASD from a normative peer sample; it demonstrates strong convergent validity with the ASSQ, which is an ASD trait questionnaire used in Finland in clinical settings with high-functioning school-aged children (29). The present study demonstrates the aggregation of autistic traits among the family members of children with ASD. Specifically, we found that the fathers and brothers (but not the mothers or sisters) of children with ASD had higher levels of autistic traits as measured by the SRS compared with their control counterparts and that, in ASD families, fathers—but not mothers—trait severity was significantly associated with child trait severity. By contrast, in the families of typically developing children, mothers’ QAT had a stronger association with child SRS scores than did fathers’ QAT.

Our analyses of the familial associations of QAT revealed that, in ASD families, child QAT was more strongly associated with paternal than maternal QAT. Elevated QAT in male but not female family members of individuals with ASD has also been demonstrated in prior literature. For example, Lyall and colleagues (15) reported a significant risk in offspring ASD on the basis of elevated SRS scores in fathers but not mothers. In their prospective longitudinal infant sibling study of familial QAT, Schwichtenberg and colleagues (14) reported the highest rates of QAT in the fathers and siblings of ASD families. Virkud and colleagues (13) also demonstrated the aggregation of subclinical autistic traits among the brothers and fathers of multiplex ASD families but not among the mothers.

In our study sample, the mothers of ASD probands did not differ significantly on any of the SRS scales from the mothers of controls; however, the sisters of children with ASD demonstrated certain differences from control girls, with significantly lower scores (indicating higher functioning) on the Social Awareness and Social Cognition subscales. One explanation for this seemingly contradictory finding is that the ability of a typically developing female sibling to adapt to a family system where there is a sibling with special needs may be enhanced. It is also possible that the low scores of the sisters of children with ASD may reflect the way parents assess their daughters with no special needs (as compared to their children with ASD). Virkud and colleagues (13) found that the aggregation of QAT was observed in only the male siblings of children with ASD, even in the multiplex families. These results may support gender differences in both QAT inheritance and diagnostic clinical practice. Moreover, as suggested by other researchers (30,31), higher levels of family QAT may be required for girls to meet clinical levels as measured by these scores. The current study did not have a sufficient sample size to fully explore gender differences with high statistical power, but these issues should be further investigated in future studies.

A recent large family study conducted by Constantino and colleagues (18) that included 1235 families and 2920 children demonstrated that the sibling recurrence of ASD varies as a function of family type (i.e., simplex vs. multiplex). QAT aggregation was found in unaffected children of multiplex ASD families but not in simplex ASD families. Consistent with this was that Schwichtenberg and colleagues (14) found infant siblings from multiplex families to be at significantly higher risk for ASD as compared with infant siblings from simplex families.

The current study excluded multiplex ASD families; however, in our sample of simplex ASD families, the brothers of children with ASD had significantly higher scores than control boys on the SRS subscale of Social Motivation. The mean difference in the SRS total score between groups was 6.8 points with a very large effect size, which suggests a clinically meaningful difference (see Table 1). In addition, contrary to the other research, we found that SRS scores in the unaffected brothers and fathers of children with ASD were not normally distributed; rather, they were skewed toward the pathological end. Gender differences emerged in the parents of children with ASD as well as in the siblings of children with ASD, with males having higher level of QAT than females in both groups. These results suggest that ASD characteristics and deficits in reciprocal social behavior may aggregate in the unaffected male family members of simplex families as well.

Overall, these results support the idea that subclinical traits assessed by the SRS may manifest more frequently or may be more notable among the male relatives of ASD probands and that elevated scores aggregate in simplex families. It is possible that females have reduced susceptibility to such ASD traits as well as reduced penetrance or expression of these traits, and they may also be rated differently by their parents as compared with their male counterparts.

Control parents did not differ with regard to their SRS scores. Moreover, contrary to the previous findings of Kamio and colleagues (11) in their nationwide study that included more than 20,000
school-aged children, we found no gender differences in the SRS scores of control children. This inconsistent finding may be the result of the limited size and homogeneity of our sample. It suggests that, among typically developing children, there are no gender differences in social reciprocal behavior development. The SRS scores were normally distributed in the control groups, which is consistent with previous findings that have demonstrated the normal distribution of ASD traits in the general population (6,8).

Lyall and colleagues (15) found evidence of family transmission of QAT in their general population control sample. Among typically developing control children in the present study, child QAT was more strongly associated with mother QAT than father QAT. This finding was particularly evident among children with the weakest reciprocal social behavior capacity (i.e., those children in the highest SRS quartile; see Figure 1). It is possible that, among typically developing children, social skills are learned via interaction with the mother, regardless of the father’s reciprocal social behavior capacity. Alternatively, these results may reflect social impairment that is not related to ASD; it has been suggested that low or moderate SRS score elevations may be present with variety of psychiatric disorders (2), and the potential for other psychopathology to influence these results cannot be ruled out. For example, SRS scores that are elevated in the range of 40 to 55 have been reported among individuals with anxiety disorders and social deficits related to attention-deficit/hyperactivity disorder (32-34). The mean SRS score of the control families of our study was less than 40, even for the families of control children in the highest quartile (see Figure 1). Thus, strong correlations between mothers and children in the control families may be the result of non-ASD psychopathology. Given the small sample size of this study, we cannot rule out chance findings, and these and other explanations should be further explored.

**Limitations**

Although the current study had a number of strengths—including the ability to examine the family transmission of SRS scores, scores in siblings, and scores by gender as well as to have detailed clinical diagnoses confirmed—several limitations should also be noted. First, the definition of a simplex family is subject to bias as a result of undiagnosed parents or siblings or potential changes with the addition of infant siblings who may later develop ASD. We selected the families on the basis of their present statuses, and we attempted to minimize such bias by inquiring about parents’ psychiatric diagnoses during the ADI-R interview and by asking parents about their developmental concerns regarding their other children. In addition, diagnostic evaluations were performed on all siblings for whom concerns were indicated. Thus, siblings in this sample with high levels of QAT either did not meet the diagnostic criteria of ASD despite high levels of quantified ASD traits, or these traits did not cause clinical impairment in their everyday lives. Because we had only parental SRS evaluations of the children, reporter bias is possible, as it is with any informant-report measure. However, Constantino and colleagues (35) have reported strong correlations between teacher and parent reports (r = 0.72), which suggests that such bias is unlikely to drive robust statistical results. We also did not conduct full psychiatric diagnostic evaluations of control families; thus, as previously mentioned, the presence of non-ASD diagnoses (e.g., major depressive disorder, anxiety disorders, attention-deficit/hyperactivity disorder) cannot be ruled out as influencing the QAT found in our control sample. Finally, we were not able to evaluate how environmental issues, such as caring for a child or children with special needs, may affect parent and sibling features as measured by the SRS. This could be addressed by including control groups of parents and siblings of children with special needs other than ASD.

**Conclusions**

**Clinical Significance**

The SRS measures different domains of reciprocal social capacity (perception, cognition, communication, and motivation) as well as the presence of restricted interests and repetitive behavior. Results from this study provide important clinical information, particularly with regard to communicating with the parents and siblings of children with ASD. For example, we should consider that the fathers of children with ASD may have difficulty with pragmatic language, joint attention, communicating their feelings to others, and maintaining conversations. Although this type of prediction is not necessary, it is important for the therapist to be aware of any possible deficits and thus monitor and adapt his or her communication style accordingly. Parents—and, again, fathers in particular—may have sensory hyperresponsiveness or hyporesponsiveness that may interfere with their ability to concentrate or that may result in tension and discomfort during social situations. The brothers of children with ASD may be at an increased familial risk for exhibiting restricted interests, stereotypic play, routine dependence, resistance to change, and mannerisms that are qualitatively similar to those seen in children with...
ASD. Moreover, they may avoid or dislike group activities, and they may hesitate to separate from their parents. This information is extremely clinically important when planning meetings with the family and devising family interventions.

Family members who demonstrate some ASD symptomatology or subthreshold manifestations of ASD symptoms may require additional support to enhance their own reciprocal social abilities to best support their children with ASD. Although the broader autism phenotype is not a diagnostic entity, assessing parent and sibling QAT could be a useful strategy for helping families with children with ASD, given that even mildly manifesting autistic traits have been found to be associated with internalizing problems, anxiety, mood disorders (36-38), attention-deficit/hyperactivity disorder symptoms (37,39,40), conduct problems (37,41), and behavioral problems (42,43) as well as problems with personal adjustment, lower self-esteem, and less self-reliance (36).

In addition to their usefulness for intervention planning, the results of this study are clinically significant as a result of their applicability to the early detection of new ASD cases. These results suggest that the infant siblings of children who have been diagnosed with ASD—especially males—may be at risk for developing ASD and should therefore be carefully followed and screened during regular check-ups by trained health care personnel to identify possible delays in reciprocal social behavior capability and to initiate early intervention. These findings also support the larger trends seen in the literature, which have demonstrated the familiaity of broader autism traits.

References


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